

PATENT COOPERATION TREATY

PCT



INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter II of the Patent Cooperation Treaty)

REC'D 20 MAY 2005

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(PCT Article 36 and Rule 70)

Applicant's or agent's file reference ON/4-32910A/P1+P2+P3		FOR FURTHER ACTION		See Form PCT/IPEA/416
International application No. PCT/EP2004/002616		International filing date (day/month/year) 12.03.2004	Priority date (day/month/year) 14.03.2003	
International Patent Classification (IPC) or national classification and IPC C07D239/48, C07D405/12, C07D403/12, C07D401/12, C07D401/14, A61K31/506, A61K35/00, A61P37/00, A61P29/00				
Applicant NOVARTIS AG et al.				
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau) a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>				
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input checked="" type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>				
Date of submission of the demand 01.10.2004		Date of completion of this report 19.05.2005		
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized Officer Telephone No. +49 89 2399- 		

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Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
 - ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-170 as originally filed

Claims, Numbers

1-22 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
 - ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
 4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
 - ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:
- ☐ the entire international application,
 - ☒ claims Nos. 14
because:
 - ☒ the said international application, or the said claims Nos. 14 relate to the following subject matter which does not require an international preliminary examination (specify):
see separate sheet
 - ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
 - ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
 - ☐ no international search report has been established for the said claims Nos.
 - ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
 - ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
 - ☐ See separate sheet for further details

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	
	No: Claims	1-22
Inventive step (IS)	Yes: Claims	
	No: Claims	1-22
Industrial applicability (IA)	Yes: Claims	1-13,15-22
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

and /or

2. Non-written disclosures (Rule 70.9)

see separate sheet

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Re Item III.

Claim 14 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V.

1. The following documents are referred to in this communication:

D1 : WO 03/018021 A1 (AMGEN INC., USA) 6 March 2003
D2 : EP 1 054 004 A1 (YAMANOUCHI PHARMA.CO., LTD., JAPAN) 22.11.2000
D3 : GHOSH D ET AL, JOURNAL OF MEDICINAL CHEMISTRY, vol. 10, no. 5,
March 1967 (1967-03), page 974, XP001000379
D4 : GHONEIM K M ET AL, JOURNAL OF THE INDIAN CHEMICAL SOCIETY,
vol. 63, no. 10, October 1986 (1986-10), pages 914-917, XP000985005
D5 : GHOSH D., JOURNAL OF THE INDIAN CHEMICAL SOCIETY, vol. 58, no.5,
May 1981 (1981-05), pages 512-513, XP000918018
D6 : WO 01/60816 A1 (AMGEN INC., USA) 23 August 2001
D7 : WO 00/39101 A (ASTRAZENECA UK LTD) 6 July 2000
D8 : WO 97/19065 A (CELLTECH THERAPEUTICS LTD) 29 May 1997
D9 : WO 01/65655 A (HYDE DOUGLAS) 7 September 2001

2. NOVELTY, ARTICLE 33(2) PCT:

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 1 is not new in the sense of Article 33(2) PCT:

- in fact, D1-D5 anticipate the subject-matter of claim 1 in that they disclose specific examples of compounds falling within the scope of current claim 1:
- in D1, Examples 67,69,70,236-240, 251 and 256.
- in D2, compounds 121-124 in Table 9, example 37 in Table 3 and examples 8,39,40 in Table 5.
- in D3, compound V of Table I.
- in D4, compounds 2a, 2b and 2d in Table I.
- in D5, compound VIII of table I.

Thus, the requirements for novelty of article 33(2) PCT are not considered to be satisfied.

3 INVENTIVE STEP, ARTICLE 33(3) PCT:

The present application does not meet the criteria of Article 33(1) PCT, because the subject matter of claim 1 does not involve an inventive step in the sense of Article 33(3)PCT:

Document D1, which is considered to represent the most relevant state of the art to the subject matter of claim 1, discloses 2,4-diamino-pyrimidines for use as anticancer agents. These compounds do not only have the same structure as the claimed compounds but also present the same biological activity, namely they are kinases inhibitors such as ZAP-70 or IGF-1R-inhibitors (see pp.186-189).

The compounds of independent claim 1 as well as their use in the treatment of a disease which responds to inhibition of FAK or /and IGF-1 receptor have been anticipated by D1. Starting from D1 and using the teachings of the prior art documents D6-D9, the skilled person, faced with the problem of providing further FAK and/or IGF-1 receptors inhibitors, would have been unambiguously led to prepare the compounds of the present application.

Thus, the underlying technical problem to be solved by the present invention may therefore be regarded as the provision of FAK or/and IGF-1 receptor inhibitors, which provide an unexpected effect with regard to the already known inhibitors of the prior art.

However, the present application contains pharmacological data, which prove that the claimed compounds are indeed FAK and/or IGF-1 receptor inhibitors (see pp.164-170) but there is no evidence for a surprising or improved effect compared to the compounds of the prior art.

It is not at present apparent which part of the application could serve as a basis for a new, allowable claim, because no difference of the subject-matter of the claims vis-à-vis the state of the art could be identified. Furthermore, there is no appropriate information that clarify where an inventive step lies in the application and which unexpected effect is associated with it.

The present application is therefore not considered to meet the criteria of Art.33(3) PCT.

Dependent claims 2-22 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step (Article 33(2) and (3) PCT).

4. INDUSTRIAL APPLICABILITY:

For the assessment of the present claim 14 on the question whether they are industrially

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applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VI

Certain documents cited

Certain published documents

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO03078404	25.09.2003	14.03.2003	15.03.2002
WO2004/002964	08.01.2004	26.06.2003	28.06.2002
WO03030909	17.04.2003	25.09.2002	25.09.2001
WO03063794	07.08.2003	31.01.2003	01.02.2002

These documents are all related to 2,4-diaminopyrimidines compounds useful as anticancer agents.